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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/938,540	08/27/2001	Bettina Moeckel	211223US0X	2794

22850 7590 08/26/2003

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EXAMINER	
FRONDA, CHRISTIAN L	

ART UNIT	PAPER NUMBER
1652	12

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/938,540	MOECKEL ET AL.	
	Examiner	Art Unit	
	Christian L Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-25 is/are pending in the application.

4a) Of the above claim(s) 8,9 and 12-25 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-4,6,10 and 11 is/are rejected.

7)☒ Claim(s) 5 and 7 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 27 August 2001 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicants' election with traverse of Group I, claims 1-7, 10, and 11, in Paper No. 11 is acknowledged. The traversal is on the grounds that the Office has not provided reasons to support a conclusion of patentable distinctness between Groups I-IV. This is not found persuasive because for reasons stated in the previous Office Action and the reasons below.

The polynucleotide, vector, and host cell of Group I and the coryneform bacterium having an attenuated ccpA1 gene of Group II are different products that require different searches since the attenuated ccpA1 gene of Group is expected to have a different nucleotide sequence/structure then that of the polynucleotide of Group I. The methods of Groups III and IV are distinct both physically and functionally; require different process steps, reagents, and parameters; and produce different products as evident by their different purposes and method steps. The product of Group II can be used in a materially different process of using that product such as using coryneform bacteria in a recombinant process for the production of the attenuated ccpA1 protein which is expected to differ in amino acid sequence/structure and function than the wild-type ccpA1 protein encoded by the polynucleotide of Group I.

A search of all the inventions in the patent literature and the non-patent literature cannot be made without serious burden because the inventions require separate searches that have different limits, boundaries, scope, and subject matter. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their divergent subject matter and classification, restriction for examination purposes is proper.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-7, 10, and 11 are under consideration in this Office Action.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 3, 4, and 6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey

to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention encompass any polynucleotide which is at least 70% identical to any polynucleotide that codes for a polypeptide comprising SEQ ID NO: 2, any polynucleotide encoding a protein comprising an amino acid sequence that is at least 70% identical to SEQ ID NO: 2, any polynucleotide that comprising at least 15 successive nucleotides of said polynucleotide, any polynucleotide which hybridizes to SEQ ID NO: 1, and any polynucleotide of "sense mutations of neutral function" of SEQ ID NO: 1. The specification, however, only provides the following representative species encompassed by the invention: an isolated polynucleotide consisting of SEQ ID NO: 1 and a polypeptide consisting of SEQ ID NO: 2. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of these polynucleotides by any identifying structural characteristics or properties for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

5. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or an isolated polynucleotide comprising SEQ ID NO: 1; does not reasonably provide enablement for any other embodiment.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claims encompass any polynucleotide which is at least 70% identical to any polynucleotide that codes for a polypeptide comprising SEQ ID NO: 2 and any polynucleotide encoding a protein comprising an amino acid sequence that is at least 70% identical to SEQ ID NO: 2.

The specification provides guidance and examples for making an isolated polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or an isolated polynucleotide comprising SEQ ID NO: 1. However, the specification does not teach the specific structural/catalytic amino acids and the structural motifs essential for protein activity/function which cannot be altered. The state of the art as exemplified by Attwood et al. (Comput. Chem. 2001, Vol. 25(4), pp. 329-39) is such that "...we do not fully understand the

rules of protein folding, so we cannot predict protein structure; and we cannot invariably diagnose protein function, given knowledge only of its sequence or structure in isolation" (see Abstract and entire publication). Furthermore, Ponting (Brief. Bioinform. March 2001, Vol. 2(1), pp. 19-29) states that "...predicting function by homology is a qualitative, rather than quantitative, process and requires particular care to be taken...due attention should be paid to all available clues to function, including orthologue identification, conservation of particular residue types, and the co-occurrence of domains in proteins" (See Abstract and entire publication).

The standard for meeting the enablement requirement is whether one of skill in the art can make the invention without undue experimentation. The amount of experimentation to make the claimed polynucleotide is enormous and entails selecting specific nucleotides to change (deletion, insertion, substitution, or combinations thereof) in a polynucleotide to make the claimed polynucleotides and determining by assays whether the polypeptide has activity. The specification does not provide guidance with respect to the specific structural/catalytic amino acids and the structural motifs essential for enzyme structure and activity/function which must be preserved. Thus, searching for the specific nucleotides to change (deletion, insertion, substitution, or combinations thereof) in a polynucleotide to make the claimed polynucleotides is well outside the realm of routine experimentation and predictability in the art of success in determining whether the resulting polypeptide has activity is extremely low since no information is provided by the specification regarding the specific catalytic amino acids and the structural motifs essential for enzyme structure and activity/function which must be preserved.

The Examiner finds that one skilled in the art would require additional guidance, such as information regarding the specific catalytic amino acids and the structural motifs essential for activity/function which must be preserved. Without such a guidance, the experimentation left to those skilled in the art is undue.

6. Claims 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the *E.coli* strain DSM13673 and vector pCR2.1ccpA1int are required to practice the claimed invention. As such the strain and vector must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 USC § 112, first paragraph, may be satisfied by a deposit of the *E.coli* strain DSM13673 and vector pCR2.1ccpA1int.

The process disclosed in the specification to make the *E.coli* strain DSM13673 and vector pCR2.1ccpA1int does not appear to be repeatable. The specification discloses a gene and plasmid vectors used to construct the *E.coli* strain and vector. However, the nucleotide

sequences of the plasmid vectors are not fully disclosed, nor have all the nucleotide sequences required for their construction been shown to be biblically known and freely available. The specification does not disclose a repeatable process to obtain the plasmid vectors and it is not apparent if the nucleotide sequences of the gene and novel vectors are readily available to the public. It is not apparent if the *E.coli* strain and vector or source material to make them are both known and readily available to the public.

Applicants' referral to deposit of *E.coli* strain on page 13, lines 11-16, in the specification is noted but is considered insufficient assurance that all of the conditions of 37 CFR 1.801-1.809 have been met. While Applicants have deposited the *E.coli* strain, there is no indication in the specification as to public availability.

If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by the applicant, or a statement by an attorney of record over his/her signature and registration number, stating that the specific microorganism has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. 1.801-1.809 and MPEP 2402-2411.05, the applicant may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his/her signature and registration number, showing that:

(1) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(2) all restriction upon availability to the public will be irrevocably removed upon granting of the patent;

(3) the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and

(4) the deposit will be replaced if it should ever become inviable.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-4 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because the specific nucleotide sequence of the polynucleotide to which the claimed polynucleotide is 70% identical to is not known and not recited in the claim. Furthermore, it is not known how a polynucleotide can encode a ccpA1 gene. Claims 2-4 which depends from claim 1 are also rejected because they do not correct the defect of claim 1.

In claim 6 (ii), the phrase "within the range of the degeneration of the genetic code" renders the claim vague and indefinite because the meaning of the phrase is not known. Claim 6 (iii) is vague and indefinite because the specific hybridization conditions are not known and not recited. In claim 6 (iv), the phrase "sense mutations of neutral function" renders the claim vague and indefinite because the meaning of the phrase is not known and the specific genetic modification(s) which results in the claimed polynucleotide being "sense mutations of neutral function" are not known and not recited.

Claim Rejections - 35 U.S.C. § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Chang et al. (Accession AF260427).

Chang et al. (Accession AF260427) teach a polynucleotide comprising at least 15 nucleotides of a polynucleotide encoding SEQ ID NO: 2 (see attached alignment).

11. Claim 6 is rejected under 35 U.S.C. 102(b) as being anticipated by Sanchez et al. (Accession AZ048854).

Sanchez et al. (Accession AZ048854) teach a polynucleotide that is expected to hybridize to SEQ ID NO: 1 since no stringent hybridization conditions have been recited (see attached alignment). Thus, the reference teachings anticipate the of claimed invention.

Conclusion

12. No claim is allowed.

13. Claims 5 and 7 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L. Fronda whose telephone number is (703)305-1252. The Examiner can be contacted Monday-Friday from 8:30AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703)308-3804. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703)308-0196.

CLF

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